

Remarks/Arguments

Claims 1, 3-5, 7, 10-13, and 30 have been amended. Claims 6 and 18 have been cancelled. The amendments are proper since they present the claims in better form for allowance or consideration on appeal. The application as presently claimed contains patentable subject matter, and allowance is respectfully requested.

Applicant's Invention

Applicants' invention is directed to a purification device including a detachable and discrete cylindrical capsule column module which can be pre-packed with wet, hydrated chromatographic media (or be supplied empty for the end-user to pack with chromatographic media) for purification of proteins, typically via centrifugation. A diverse selection of chromatographic media can be exploited in these column modules, thereby creating kits bundled with buffers and sample preparation tools that provide the total purification solution to the end-user. The columns can be inserted into the sample chambers through a compression fit. The detachability of the column modules enables the very same column modules to be re-used. The column modules are capsules, and as such are capped at both ends so that the media is preserved with an extended life span and shipped *in situ*. The capsule is an innovative feature which allows wet chromatography media to be stored in the column module without deterioration in performance.

A sample chamber (i.e., reservoir) resides above the cylindrical capsule column module, and a lower tapered part of the sample column module holder houses the cylindrical capsule and is intended to enhance the separation power of the column in a centrifuge. The purification device operates under low pressure separation processes. The detachable cylindrical capsules contain a microporous flow regulator that regulates the flow rate of the sample through the column module. Increasing the residence time through the chromatographic media in the column module increases significantly the binding capacity of the column. The slowest speed generated by a centrifuge, for example, is typically too fast for the binding kinetics of many porous media.

The invention is relevant to single array or multiple array formats where multiple samples can be processed in parallel.

The Cited Prior Art

U.S. Patent No. 5,918,273 (Horn)

The Horn Patent is directed to a cassette assembly for loading samples for use in applications of high performance liquid chromatography (HPLC), an analytical method which requires high pressure conditions where small liquid samples are atomized and passed through a column. It is comprised of mini-columns which possess required concave ends, and sample loading funnels included therein for loading and providing a specimen for analysis by HPLC. The concave ends of the mini-columns create an interface which permits direct insertion of the mini-column into a high pressure solvent line suitable for performing HPLC.

U.S. Patent No. 6,103,195 (Shukla)

The Shukla patent is directed to the use of spin columns for a centrifuge using a conventional luer lock configuration to prepare and purify a variety of compositions. More than one spin column is required, and the spin columns spaced above and below each other. Filtration and a chromatographic procedure are performed in a two-part process by the different columns.

U.S. Patent No. 5,603,899 (Franciskovich)

The Franciskovich patent is directed to a multiple column chromatography assembly including a manifold with a plurality of support tubes and a plurality of separation columns placed in the support tubes.

Rejections Under 35 U.S.C. §112

Reconsideration is requested of the rejection of claims 1 and 3-12 as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant has amended claim 1 to include a "column insert portion" as a claimed element, and has eliminated the limitation "securable to the purification device," per the examiner's suggestion. The amendments do not change the scope of the claims in any way, and one of ordinary skill in the art would have understood the claims as previously presented.

Amendments to dependant claims 3, 5, and 7 have also been made in order to clarify the dependency of elements. Any asserted inconsistency in language was not such that one of

ordinary skill in the art would not have understood the scope of the claim. The claims, although objectionable in their original form, were not rejectable under section 112. Should the examiner disagree with this distinction and remain of the opinion that the appropriate manner to deal with the claims was by section 112 rejection, and not by objection, it is requested that applicant be so advised. Otherwise, applicants will assume that the examiner agrees with applicants' position.

Rejections Under 35 U.S.C. §102

Anticipation under 35 U.S.C. §102 requires each and every limitation of the claim to be disclosed in a single prior art reference, either expressly or inherently. The anticipating reference must disclose the elements in the arrangement called for by the claim. If any limitation of the claim is missing, the reference does not anticipate.

Reconsideration is requested of the rejection of claims 1-5, 7, 10-11, 13, and 17-18 as anticipated by Horn. Horn fails to disclose a "permeable membrane configured to contain a medium and permit passage of a sample through the medium." Horn therefore fails to anticipate the presently claimed invention. Horn also fails to disclose a "discreet column insert module comprising a cylindrical capsule extending from an opening of the sample chamber." A cylinder is a shape defined by "a surface generated by a straight line moving parallel to a fixed straight line and intersecting a plane curve." See *Webster's II New Collegiate Dictionary*, 1995. The surface of the presently claimed column insert module is cylindrical, and is therefore a straight line extending from the opening of a sample chamber.

Horn's mini-column, in contrast, is required to have concave tapered ends, and is not cylindrical. Horn does not disclose a cylindrical capsule as presently claimed, but rather discloses "a generally concave, preferably tapered opening at each end of the column." See column 5, lines 15-17 of Horn. The ends are tapered, or as Horn teaches, concave, to ensure zero dead volume and a suitable high pressure seal with a compression fit to a conical tip nozzle.

Further, the mini-column of Horn is not a capsule. The invention of Horn is restricted to mini columns that are not capped. The presently claimed column insert module is a cylindrical capsule, and thus is capped at its ends and is used for packing both soft and hard resin slurries in a hydrated and wet state. There is no such cylindrical capsule in the Horn patent.

The examiner states that feature 52 in the present application precludes applicants' module from being cylindrical, and further states the external flange 41 of Horn is analogous to element 52 of the present application. Applicants respectfully disagree. Element 52 in fact provides the claimed cylindrical capsule structure by capsulating the cylinder. External flange 49 of Horn does not provide any capsulation to Horn's column and is not analogous to element 52 of the application.

Furthermore, the assembly of Horn requires a non-cylindrical construction including concave ends in order to function properly. Horn clearly states in column 5, lines 10-19, that "unlike the mini-columns of the prior art, both terminal ends of the mini-columns of this invention are designed to accommodate the extremely high pressures (greater than 1200 psi) needed to perform reverse-phase HPLC of the immobilized proteins or other hydrophobic moieties. This is accomplished by designing a generally concave, preferably tapered opening at each end of the column so that an interface means may be attached thereto with near-zero dead volume." The mini-columns are used for extremely high pressure needed to perform reverse phase HPLC. The present invention relates to low pressure applications, such as centrifugal and chromatographic operations not related to high performance liquid chromatography (HPLC), and does have tapered ends.

Each of the independent claims include a "discreet column insert module comprising a cylindrical capsule extending from an opening of the sample chamber" and a "permeable membrane" as defined in claim 1, and each independent claim and claims dependent therefrom are not anticipated for the same reasons.

Rejections Under 35 U.S.C. §103

Reconsideration is requested of the rejection of claims 6-9, 12, 14-16, and 31-34 as defining subject matter that would have been obvious in view of Horn combined with U.S. Patent No. 6,103,195 to Shukla for claims 6-9 and 12; and U.S. Patent No. 5,603,899 to Franciskovich for claims 14-16 and 31-34. Each of these claims contains the "discreet column insert module comprising a cylindrical capsule extending from an opening of the sample chamber and configured to contain a separation bed," which is neither disclosed nor suggested in Horn. Neither Shukla nor Franciskovich disclose such a cylindrical capsule, and the combination of the references therefore fail to render the present invention obvious under 35 U.S.C. § 103.

Further and with regard to the “permeable membrane” element added to the independent claims, Horn and Shukla are not combinable in order to render the present invention obvious. Whether or not disclosures in two or more prior art references are properly combinable depends, generally, on whether there is some teaching or suggestion in those references or elsewhere in the prior art to suggest the desirability of making the combination. The mere fact that it is possible to find two isolated disclosures having some individual features that might be combined in a manner that would result in the claimed invention is not enough. There must be something in the prior art itself that suggests the desirability of the claimed combination. See *In Re Fine*, 5 USPQ2d 1596, 1599 (Fed. Cir. 1998).

In the present case, not only is there no motivation to combine Horn and Shukla, but even if combinable, they would not render the present invention obvious. A mini-cassette for a HPLC column would not be substitutable for a centrifuge column. The two function in entirely different manners, and one of skill in the art would not look to the other for modifications or improvements. High performance liquid chromatography is a process where an analyte is forced through a column of a stationary phase in a solvent (mobile phase) at high pressure, which decreases the time the separated components remain on the stationary phase and thus the time they have to diffuse within the column. HPLC instruments consist of a reservoir of mobile phase, a pump, an injector, a separation column, and a detector. Compounds are separated by injecting a plug of the sample mixture onto the column. The different components in the mixture pass through the column at different rates due to differences in their partitioning behavior between the mobile phase and the stationary phase.

Horn teaches mini-cassettes for use with HPLC analysis. One of skill in the art would not look to Shukla, which relates to a spin column for use with centrifuge processes to improve the mini-cassettes of Horn. More importantly, one cannot combine the non-analogous references to arrive at the claimed invention as HPLC and centrifuge process are entirely different separation processes with different requirements and considerations for each.

The application is considered to be in condition for allowance, which action is solicited.
Enclosed is a request for a one month extension of time.

Respectfully submitted,



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